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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/233,218	01/20/1999	CLAIRE A CAJACOB	04983.0025.U	7809

28381 7590 11/28/2003

ARNOLD & PORTER
IP DOCKETING DEPARTMENT; RM 1126(b)
555 12TH STREET, N.W.
WASHINGTON, DC 20004-1206

EXAMINER	
KIM, YOUNG J	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 11/28/2003

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 11062003

Application Number: 09/233,218
Filing Date: January 20, 1999
Appellant(s): CAJACOB ET AL.

Holly Logue Prutz
Danielle M. Edwards
David R. Marsh
Lawrence M. Lavin, Jr.
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 06/27/2003.

(1) Real Party in Interest

A statement identifying the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

(3) Status of Claims

The statement of the status of the claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Invention

The summary of invention contained in the brief is correct.

(6) Issues

The appellant's statement of the issues in the brief is correct.

(7) Grouping of Claims

The rejection of claims 1 and 10-23 stand or fall together because appellant's brief does not include a statement that this grouping of claims does not stand or fall together and reasons in support thereof. See 37 CFR 1.192(c)(7). Although Appellants have stated that the separate patentability of claims 1 and 10-22 were addressed together, this is not an express statement regarding whether the claims stand or fall together.

(8) Claims Appealed

The copy of the appealed claims contained in the Appendix to the brief is correct.

(9) Prior Art of Record

Iyers et al., "Quod erat demonstrandum? The mystery of experimental validation of apparently erroneous computational analyses of protein sequences" Genome Biology, vol. 2, no. 12, (Nov 13, 2001), pp. 1-11

(10) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1 and 10-23 were rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The Advisory Action mailed out on April 21, 2003 as well as page 3, 1st paragraph of Final Action mailed out on January 27, 2003 clearly states the inclusion of claims 1, 10, 22, and 23 in the rejection under the above statute.

With regards to Appellants' statement in the Brief received on July 2, 2003 (page 5, 2nd paragraph), wherein the Appellants state that, "claims 11-21 and 23 do not include the recitation of nucleic acid molecule that encodes a maize tetrapyrrole pathway enzyme or fragment thereof and therefore should not have been rejected in accordance with the Examiner's statement that the 'enablement argument will be drawn to whether or not the claimed nucleic acids do in fact encode a functional glutamyl-tRNA reductase,'" Examiner withdrew the prior utility rejection of claims 11-21 under 35 U.S.C. 101 based on the finding that the claimed polynucleotides of the claimed SEQ ID Numbers were disclosed (page 255, specification) as having ***at least one***

substantial utility based on their homology to the glutamyl-tRNA reductase (page 2, 3rd paragraph, Final Action mailed out on January 27, 2003). However, based on the determination that the claims 11-21 as well as the newly submitted claims 22 and 23 (page 2, 1st paragraph, Final Action mailed out on January 27, 2003) do not enable a skilled artisan to make and/or use the invention as glutamyl-tRNA reductase, the rejection under 35 U.S.C. 112, first paragraph have been made.

Claims 1, 10, and 11-22 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The rejection of the newly submitted claim 22 is clearly stated in page 6, 2nd paragraph of the Final Office Action mailed out on January 27, 2003.

(11) Response to Argument

The specification is Not Enabling for the Scope of the Claimed Nucleic Acid Molecules

Preliminarily, Appellants' statement regarding the typographical error of including claim 2 in the enablement rejection is correct. Claim 2 had been cancelled without prejudice to or disclaimer in the Amendment received on November 12, 2002.

With regard to Appellants' remark regarding the citation of *Ex Parte Lemak*, the citation of the case includes 210 USPQ 306, and 307. Upon retrieval of the 307 case, Examiner found that the case was not directed to *Ex Parte Lemak*, but *Warnaco Inc. v. Adventure Knits, Inc.*

Appellants state that the Office has not met the evidentiary burden to impose an enablement rejection, nor has the Examiner presented evidence to suggest that one skilled in the

art would doubt the claimed nucleic acid molecules would encode a maize glutamyl-tRNA reductase enzyme or fragments thereof. Whether or not a skilled artisan would believe the Appellants' assertion is reserved for assessing the credibility of the asserted utility. The utility requirement, however, is not the subject of the argument.

Further, Appellants state that in light of the After Final Amendment received on April 7, 2003, the amendment to claim 1 (and its dependent 10 and 22) which removes the phrase, "that encodes a maize glutamyl-tRNA reductase enzyme or fragment thereof," renders moot the rejection of claims 1, 10, and 22 under 35 U.S.C. 112, first paragraph, (page 5, 1st paragraph; Brief). However, the rejection of claims 1, 10, and 22, as well as the remaining claims 11-21 and 23 under 35 U.S.C. 112, 1st paragraph was not based on the explicit citation of the above phrase which was removed by Appellants' Amendment, but because it was determined that the specification did not enable a skilled artisan to make and/or use the claimed invention for which at least one asserted utility was found to be substantial. Therefore, the enablement issues regarding claims 1, 10 and 22 are not rendered moot and will be addressed in the instant Answer.

Appellants state that it is unclear why the Office maintains the enablement rejection for claims 11-21 and 23 when the claims make no recitation of "a nucleic acid molecules that encodes a maize tetrapyrrole pathway enzyme of fragment thereof" (page 5, Brief) and since claimed nucleic acid molecules are "useful as markers and probes...obtain nucleic acid homologues...identify the presence or absence of polymorphisms..." (page 5, 3rd paragraph, Brief).

As evident from the prosecution history, claims 11-21 (prior to addition of claim 23) have been initially rejected under 35 U.S.C. 101 for lacking patentable utility. In that Office Action

(mailed out on August 14, 2002), the claims were rejected for lacking patentable utility with regards to their use as markers, probes, identifying homologues, detection of polymorphisms, etc. (pages 3-7). Examiner withdrew the prior utility rejection of claims 11-21 under 35 U.S.C. 101 ***based on the finding*** that the claimed polynucleotides of the claimed SEQ ID Numbers were disclosed (page 255, specification) as having ***at least one substantial utility*** based on their homology to the glutamyl-tRNA reductase (page 2, 3rd paragraph, Final Action mailed out on January 27, 2003). However, based on the determination that the claims 11-21 as well as the newly submitted claims 22 and 23 (page 2, 1st paragraph, Final Action mailed out on January 27, 2003) do not enable a skilled artisan to make and/or use the invention as glutamyl-tRNA reductase, the rejection under 35 U.S.C. 112, first paragraph have been made.

On page 6, 1st and 2nd paragraphs of the Appellants' Brief, it appears that Appellants are arguing the enablement of the embodiments which were rejected for lacking patentable utility. As already stated above, the enablement with respect to the embodiment which met the utility requirement, that is, the embodiment of the nucleic acid which encodes a glutamyl-tRNA reductase, is being considered.

Appellants state that a reasonable analysis of the *In re Wands* criteria supports Appellants' position that no undue experimentation would be required to make and use the claimed invention (page 6, bottom, Brief).

The only evidence provided by the specification is the result of BLAST™ on the claimed SEQ ID Numbers (page 255, specification), the homology of which are listed below:

SEQ ID NO	Homology	Characterized As
586	83%	maize glutamyl-tRNA reductase

590	85%	maize glutamyl-tRNA reductase
594	82%	maize glutamyl-tRNA reductase
596	86%	maize glutamyl-tRNA reductase
597	87%	maize glutamyl-tRNA reductase
599	87%	maize glutamyl-tRNA reductase
600	86%	maize glutamyl-tRNA reductase
601	84%	maize glutamyl-tRNA reductase
604	86%	maize glutamyl-tRNA reductase
605	89%	maize glutamyl-tRNA reductase

Examiner finds no other evidence in the specification nor by the Appellants other than Appellants' assertion based on the above homology.

Appellants argue that the first *Wands* criteria, which is the quantity of experimentation necessary, would not be undue because the, "'make-and-test' quantum of experimentation is reduced by the extensive knowledge, *e.g.,* of conservative nucleotide substitutions, identification of an active site..." (page 7; Brief). However, such knowledge has not been demonstrated in this case. The specification does not identify any of the functional conserved domain across the species of the glutamyl-tRNA reductase (Glu TR hereon) to reasonably convey to one skilled in the art that the claimed polynucleotide does, in fact, encode a Glu TR nor how its encoded protein would share these conserved domains. The specification also fails to identify the so-called, "active site" within the claimed polynucleotide. Additionally, not only does the specification lack complete open reading frame of the claimed nucleic acids, but its also lacks

information on what region of the claimed sequences is drawn to the functional domains of the Glu TR.

Appellants argue that the second and third *Wands* criteria, which relates to the amount of guidance given and the presence or absence of working examples, have been fulfilled. This is not the case in the present application. The only guidance which the specification contains is the fact that the claimed nucleic acids share "sequence homology" to known nucleic acids encoding Glu TR of known species. However, the specification does not identify what region is the coding region, or functionally conserved region. It is also interesting to note how Appellants refer to the specification wherein it recites that the purified barely Glu TR has a molecular weight of 270 kD with a monomeric subunit size of 54kD, but fail to state whether the same subunits are present in claimed nucleic acids. The specification also **lacks the actual example** which would demonstrate that the protein encoded by the claimed nucleic acid *has* the Glu TR activity. Therefore, a skilled artisan can only conclude from the specification and evidence of record that Appellants are relying solely on the BLAST™ sequence homology search.

As to the fourth, fifth, sixth, as well as the seventh *Wands* criteria which focuses on the nature of the invention and its predictability, as previously cited, Iyers et al. indicates the **status of the current art**, wherein the artisans ***clearly demonstrate*** that the practice of assigning protein functions purely based on its percent similarity to a known protein is ***unpredictable***:

> "Despite these achievements [in computational predictions], detection and interpretation of relationship between homologous proteins that have limited sequences similarity remains a ***major challenge***. Such studies typically requires a case-by-case approach that

is ***guided by a detailed understanding of protein sequence-structure patterns***."

(emphasis added)

As Iyers et al. clearly indicate, for every sequence-functional correlation, there must be a detailed understanding of protein sequence-structure patterns, to which the instant specification lack or Appellants are unable to provide.

Iyers et al. continue to state that, "[t]he negative ***feedback from experiments that failed to confirm a computational prediction is potentially even more important, because it could result in revision and refinement of the computational methods***," demonstrating the presence of unpredictability in computational assignment of protein functions ***solely*** based on sequence homology.

Clearly, Appellants have failed to disclose or guide by additional evidence (such as identification of the conserved functional domain, actual encoded protein exhibiting Glu TR acitivity, etc.) for a skilled artisan to make and use the claimed polynucleotides as a polynucleotide which encodes Glu TR. Appellants are solely relying on the very technique of assigning function based on the sequence homology, to which, at the time the application was filed, as demonstrated by Iyers et al., is determined to be unpredictable and remains a ***major challenge***.

Therefore, based on the above reasons, Examiner maintains that it would require undue experimentation of a skilled artisan to make and/or use the claimed polynucleotides as a polynucleotide which encodes Glu TR.

The Specification does NOT provide an Adequate Written Description

Appellants state that, "a person of ordinary skill in the art would, after reading the specification, understand that the inventors had possession of the claimed invention even if every nuance of the invention was not expressly described." (page 9, 2nd paragraph; Brief). Appellants argue that since Appellants have provided a nucleic acid sequence consisting of SEQ ID NO: 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605, and vectors comprising the nucleic acid sequence, as well as other systems such as BIBAC that may be used to introduce the claimed nucleic acid into a host cell, they have established possession of the claimed invention.

The claimed invention, which is drawn to a polynucleotide *comprising* the above SEQ ID Numbers, when the specification only discloses a partial sequence, as well as partial open reading frame, effectively encompasses a full-length cDNA sequence comprising a full open reading frame. While it is acknowledged that Appellant need not describe "every nuance" of the claimed invention, the written description must bear a reasonable correlation to that which is claimed. The disclosed subgenus and species embraced by the claims are not representative of the entire genus being claimed. The genus of nucleic acid molecules being claimed embraces any and every type of nucleic acid molecule that comprises any of claimed SEQ ID Numbers, and additional sequences of any size and sequence, not just vector backbones. Clearly, at the time of filing, Appellant was not in possession of genomic materials that contain the common EST fragment, which are embraced by the open-ended claims.

On page 11, 1st paragraph of the Brief, Appellants indicate that the specification describes enzymes encoded by the nucleic acid of the present invention. However, in fact, the specification does not provide any evidence that Appellants had possession of the enzymes

which are asserted to be encoded by the claimed polynucleotide. The specification only states that the claimed polynucleotide encodes a Glu TR enzyme, but fails to disclose where the open reading frame begins on the claimed SEQ ID Numbers. Appellants' assertion that the claimed polynucleotide encodes the above enzyme is solely based on homology. No evidence has been provided for a skilled artisan to recognize that Appellants had possession of a polynucleotide comprising a full open reading frame which would encode a functional enzyme.

Additionally, one skilled in the art would reasonably conclude that the claims embrace full length mRNAs, cDNAs and genomic sequences, and the specification provides no physical (i.e. structural) characteristics of these molecules to distinguish them from other nucleic acid molecules comprising the claimed SEQ ID Numbers, and no other indication that would suggest Appellant possessed them. This particular subgenus embraced by the claims has a disclosed potential utility not possessed by those members of the claimed genus useful only in hybridization. Full length mRNAs, cDNAs and genomic sequences (genes) would encode the corresponding protein(s).

A fundamental issue here is specific to the very narrow class of product that is nucleic acid molecules. The basic question upon which Appellants and the Examiner disagree is whether the disclosure of a partial sequence of nucleic acid molecules that may encode a corresponding protein is sufficient to establish possession of a broad genus based solely on the description of the partial sequence.

As stated in *University of California v. Eli Lilly and Co.* at page 1404:

> An adequate written description of a DNA ... "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. *Fiers v. Revel*, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." *Id.* at 1170, 25 USPQ2d at 1606.

That Appellants claims embrace nucleic acid molecules that encode a corresponding protein, is clearly evident from the claim language chosen. The Court in *University of California v. Eli Lilly and Co.*, at page 1405, further noted regarding generic claims:

> A written description of an invention involving a chemical genus, like a description of a chemical species, "requires a precise definition, such as by structure, formula, [or] chemical name," of the claimed subject matter sufficient to distinguish it from other materials. *Fiers*, 984 F.2d at 1171, 25 USPQ2d at 1606; *In re Smythe* , 480 F.2d 1376, 1383, 178 USPQ 279, 284-85 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus. . . .").

In the instant case, the only species specifically enumerated are the nucleic acid molecules of SEQ ID Numbers 586, 590, 594, 596, 597, 599, 600, 601, 604, and 605. The specific embodiments that in addition to these sequences include nucleic acids that will allow the corresponding protein to be encoded cannot be predicted without the coding sequence itself. This coding sequence ***has not been*** disclosed. Clearly, the specification would not show one skilled in the art that the these desired subcombinations were possessed by Appellant, and thus the embracing genus was also not possessed.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

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November 14, 2003

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